REMARKS

FORMAL MATTERS:

Claims 27-29, 31-39, 41-43, 45-49, 52, 54-72 are pending after entry of the amendments set forth herein.

Claims 1-26, 30, 40, 44, 50-51, and 53 are canceled without prejudice.

Claims 27, 38, 45, 52, 54, 56, and 57 are amended. New claims 58-72 are added. Applicant notes that new claims 59, 61, 63, 65 and 67 recite that the preserved, isolated vessel is produced from a vessel isolated from human umbilical cord, and that new claims 60, 62, 64, 66 and 68 recite that the preserved, isolated vessel is produced from a vessel isolated from human placenta. Support for these amendments and new claims is found throughout the specification, as well as in the clams as originally filed and /or previously presented.

No new matter is added.

INTERVIEW SUMMARY

Applicant is grateful to Examiner Isabella for his careful consideration of the present claims, and for the teleconference with the undersigned on January 12, 2007 regarding the status of the application and the claim rejections. During this interview, the rejections of the claims based on the prior art, as well as rejections under §112, first and second paragraphs were discussed. Amendments were proposed to address the §112, first and second paragraph rejections, which are presented here. Amendments to the claims to avoid the rejections under §102(b) were proposed during the teleconference, and are presented here for the Examiner's consideration. Applicant was encouraged to present additional evidence in support of the patentability of the claims under §103(a) in view of the cited art. Such evidence is submitted with this amendment.

RESTRICTION

Claims 48-49

The Office Action indicates that claims 48 and 49 remain directed to an independent or distinct invention on the grounds that the method claims do not require the specific product of claims 27-47, and further the product claims 27-47 may be used in a different method than that set forth in claims 48 and 49. This restriction is respectfully traversed.

Each of claims 48 and 49 depend or ultimately depend from claim 38. Thus claims 48 and 49 *necessarily* incorporate the limitations of claim 38. Claims 48 and 49 thus do require the specific product of a claim currently under examination.

Applicants' respectfully request that claims 48 and 49 be considered on the merits in the next action.

Claims 54-57

The Office Action indicates that claims 54-57 are directed to a new combination of a canister, vacuum seal, preserved vessel and removable stent not previously considered, and thus treated claims 54-57 as being directed to a non-elected invention and withdrew the claims from consideration. This withdrawal from consideration was based on the assertion that claims 54-57 do not require the graft of claims 27-37. This restriction is respectfully traversed.

Claims 54-57 depend or ultimately depend from claim 27. Thus claims 54-57 *necessarily* incorporate the limitations of claim 27, and thus do require the graft of claim 27, a claim currently under examination.

Applicants' respectfully request that claims 54-57 be considered on the merits in the next action.

New claims 68 - 72

Newly presented method claims 68-72 require all limitations of the preserved vessel of, for example, claim 38. Accordingly, examination of method claims 68-72 with the pending claims currently under examination is proper.

REJECTIONS UNDER §112, ¶1

Claims 27, 38, 50, 51, 52 are rejected under 35 U.S.C. §112, first paragraph because the specification, while being enabling for the recitation of "low antigenicity" does not reasonably provide enablement for "high patency and integrity."

Claims 27, 38, 50, 51, 52 were also are rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement.

Without conceding as to the correctness of these grounds of rejection, these rejections are rendered moot in view of the amendments presented above.

Withdrawal of the rejections of the claims under §112, ¶1 for enablement and written description is respectfully requested.

REJECTIONS UNDER §112, ¶2

Claims 30 and 40 are rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the invention.

Without conceding as to the basis for this rejection, it is rendered moot in view of the cancellation of claims 30 and 40. Withdrawal of this rejection is respectfully requested.

REJECTIONS UNDER §102

Claims 38 and 52 are rejected under 35 U.S.C. §102(b) as being anticipated by Dardik et al. (USP 3,894,530). This rejection is respectfully traversed as applied and as it may be applied to the pending claims.

The Office Action states at page 6:

> Dardik, et al discloses a preserved vessel suitable for implantation as a vascular graft produced by direct freeze-drying without chemical denaturing of a vessel isolated from a human umbilical cord or human placenta, wherein the preserved vessel exhibits low antigenicity and the preserved vessel being substantially free of fetal blood.

The Action does not point to the portion of Dardik in support of this statement.

On review of Dardik, Applicant respectfully submits that support for this assertion can not be found. Although Dardik mentions freeze-drying among a list of various treatments that could be used for preservation *of the umbilical cord as a whole*, there is no disclosure of an *isolated* preserved vessel where "the *isolated vessel* is directly lyophilized (freeze dried) without chemical denaturing". Instead, Dardik provides a laundry list of different possible treatments. See Dardik at col. 1, line 54 to col. 2, line 9:

> The umbilical cord may be used fresh or as a stored homograft (frozen or in a preservative). It may require treatment with antibiotics or other chemicals or drugs and x-ray treatment for sterilization. It may be antigenic and require treatment, for example with enzymes, to remove any antigenic substances. The cord may be freeze dried or stored in a cold environment or preserved in other known ways as to be used as an autograft if necessary for the baby whenever needed at a future date.

There is no direction in Dardik to prepare a preserved *vessel* from a vessel *isolated* from a human umbilical cord or human placenta suitable for implantation in an adult human as required by the claims. Further, there is no teaching in Dardik to use freeze-drying to the exclusion of chemical treatment, as also required by the claims.

The only other guidance in Dardik is provided in the sole working example at col. 2, line 49 to col. 3, line 22:

> During preparation of the abdominal aorta of the baboon, another investigator had taken the umbilical cord of an infant (human) that had been born two hours prior to the surgical intervention of the baboon. The cord had been delivered and taken in its entirety and transported in sterile saline solution, packed in ice. The purpose of freezing the umbilical cord in ice was to prevent any further decomposition of the cord structure. The cord, prior to insertion, was washed and irrigated numerous times with sterile Collins solution with antibiotics, in this particular instance, 1 percent cephalosporin solution and 25,000 units of bacitracin per liter of solution. The blood was thoroughly washed out from within the vessels of the cord and the cord was also irrigated with a 1 percent heparin anticoagulant solution. Following this thorough cleansing of the cord, one end of the umbilical vein within the cord which was to be used as the transplant was clamped with a clamp and through the

> other end a red rubber catheter, No. 14 French, was introduced and the vein was distended. At this point a suitable segment of umbilical graft, approximately 5 centimeters in length, was selected for excision. This segment of cord was then sterilely handled and placed into the operating field. At this point the animal was heparinized with 2,500 units of aqueous heparin given intravenously. The abdominal aorta was then clamped proximally and distally to the segment to be resected. A segment of approximately 3 centimeters in length was resected from the abdominal aorta and an end-to-end anastomosis was performed between host aorta and donor umbilical vein, first using continuous 6-0 prolene suture which is a nylon monofilament suture. The distal anastomosis was then performed following flushing of the aorta to rid it of any clot material and debris. Following completion of anastomosis the distal and then the proximal clamps were removed. It was noted that there was no bleeding between the interstices of the sutures, which is unusual, and is felt to be due to the strength and self-sealing gelatinous qualities of the cord structure. I

(emphasis added)

Thus, in the sole working example, Dardik at best discloses that the vein to be used is still in the umbilical cord segment and is not removed and/or isolated from the umbilical cord segment *prior to* performing the anastomosis at the time of implantation.

Notably, Dardik points to the "strength and self-sealing gelatinous qualities of the cord structure" as responsible for the "unusual" feature that there was "no bleeding between the interstices of the sutures". As concluded by Dr. Schneider in his analysis of the Dardik disclosure as set out in the Schneider Declaration, Dardik does not instruct or suggest isolating an umbilical cord vessel and preserving it separately from the umbilical cord. Instead, Dardik instructs one to use the vessel as part of a "suitable segment of umbilical graft" or "segment of cord". As set out in the Schneider Declaration, this would instruct one not to isolate vessels separate from the umbilical cord and preserve the isolated vessel, as such a method would not take advantage of the "strength and self-sealing gelatinous qualities of the cord structure".

Dardik fails to disclose:

- *isolating* a vessel from human umbilical cord, and
- preserving that *isolated vessel by direct lyophilization without chemical denaturing.*

Instead, Dardik, at best, discloses preserving *the entire umbilical cord* – and fails to provide any direction to preserve even the entire umbilical cord by lyophilization without chemical denaturation.

Dardik also fails to disclose isolated, preserved human *placental* vessels. Dardik only discusses umbilical cord. Dardik is silent with respect to human placenta as a source of vessels. Thus, Dardik can not anticipate the presently pending claims that are limited to use of human placenta as a source of the preserved, isolated vessel.

The above arguments notwithstanding, claims 38 and 52 as now pending recite that the preserved vessel comprises a removable stent located in its lumen. This element is not disclosed or suggested in Dardik.

Withdrawal of this rejection is respectfully requested.

REJECTIONS UNDER §103(A)

The claims are variously rejected under §103(a) based on various combinations of the disclosures of the cited references Pratt,[1] Dardik, and McDonald (US 6,090,136). Before turning to the substance of the rejections, a brief review of the law of obviousness is provided below.

As set out in MPEP § 2141 (I),[2] the four factual inquires for determining obviousness are as follows:

> (A) Determining the scope and contents of the prior art;
> (B) Ascertaining the *differences between the prior art and the claims in issue*;
> (C) Resolving the level of ordinary skill in the pertinent art; and
> (D) Evaluating evidence of secondary considerations.

(emphasis added)

The differences between the claimed invention and the prior art be evaluated "at the time the invention was made" in order to avoid impermissible hindsight. Furthermore, analysis of obviousness requires consideration of the claimed invention as a whole,[3] as well as consideration of the *entire* disclosure of

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[1] "Pratt" refers to the following publications: Laryngoscope 96:1986; and 29th Ann. Meeting of Amer. Society for Head and Neck Surgery: 1987.:

[2] Citing *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966).

[3] See, *e.g.*, MPEP § 2141.02 (I).

any prior art reference applied against the claims, including portions that would lead away from the claimed invention.[4]

The Federal Circuit developed the teaching-suggestion-motivation (TSM) test in order to assist application of the law of obviousness while avoiding hindsight. Under the TSM test, three basic criteria are required in order to establish a prima facie case of obviousness:[5]

1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.
2) there must be a reasonable expectation of success.
3) the *prior art reference (or references when combined) must teach or suggest all the claim limitations*.

(emphasis added)

The teaching or suggestion to make the claimed combination must be found in the prior art, and can not based on applicant's disclosure in order to avoid impermissible hindsight.[6]

Recently, in *KSR v. Teleflex,*[7] the Supreme Court reviewed the TSM test. While the Court warned against its "rigid application",[8] the Court also found that the TSM test could provide a "helpful insight" in determining whether the claimed subject matter is obvious under §103(a).[9] The Court in *KSR* repeatedly emphasized that an obviousness inquiry must take into account the predictability of the field:[10]

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[4] See MPEP § 2141.02 (VI) ("A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.").

[5] MPEP § 2142.

[6] *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

[7] *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (U.S. 2007).

[8] *KSR*, slip op. at 15.

[9] *KSR* slip op. at 14. *See also*, Memorandum to Technology Directors from Margaret A. Focarino, Deputy Commissioner for Patent Operations, May 3, 2007.

[10] *KSR*, slip op. at 13. (citations omitted)

> If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. *Sakraida* and *Anderson's-Black Rock* are illustrative—a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

(emphasis added)

Furthermore, when considering the Federal Circuit's application of the "obvious to try" standard to the adjustable gas pedal invention at issue, the Court stated:[11]

> l). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103.

(emphasis added)

We now turn to the rejections of record.

Claims 27-34 and 38-44 -- Pratt in view of Dardik and further in view of McDonald

Claims 27-34 and 38-44 are rejected under 35 U.S.C. §103(a) as being unpatentable over Pratt (Laryngoscope 96:1986 ("Pratt 1986"); and 29th Ann. Meeting of Amer. Society for Head and Neck Surgery: 1987 ("Pratt 1987")) in view of Dardik (US 3,894,530) and further in view of McDonald (US 6,090,136). This rejection is respectfully traversed as applied, and as it may be applied to the presently pending claims.

[11] *KSR*, slip op. at 17.

A basic requirement for a *prima facie* obviousness is that the combined disclosure must teach or suggest *all claim limitations*.[12] We first consider the disclosures of each reference, then discuss the effect of the combined disclosures.

The Office Action cites the Pratt 1986 and Pratt 1987 publications (referred collectively as "Pratt") for the following asserted disclosure:[13]

> The publications to Pratt discloses the use of freezed-dried microarterial allografts that have reduced immune response and good patency when implanted. In each of the publications, Pratt suggests that free dried placental vessels should be explored as microarterial allografts. Pratt, on page 628, discloses that a similar study by Chow, using freezed dried placental heterograft/allograft vessels as vascular substitute. The venous allograft was not harvested from a placental source, however it is clear from the studies by Pratt and Chow that freeze dried tissues exhibit low antigenicity and as, allografts, good patency. The basic question remains would it have been obvious to one with ordinary skill in the art to harvest venous from placental tissues.

(Applicant respectfully notes for the record that neither Pratt nor Chow used freeze-dried allografts using vessels from a placental source.) The Office Action then turns to the disclosure of Dardik, stating:[14]

> The earliest of Dardik, et al work teaches that placental and umbilical tissues have been used as a source for microarterial vessels for reconstructive surgery. In fact, Dardik teaches that these vessels may be freeze-dried prior to use. In light of the teachings of Dardik, et al, i.e. the use of vessels derived from placental and/or umbilical tissues as a source of microarterial allografts that can be freezed-dried to yield a reconstructive allograft that exhibits low immune response would have been obvious to one with ordinary skill in the art at the time of the invention thereof.

Finally, McDonald is cited for its disclosure of a removable stent.

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[12] MPEP §2143.
[13] Office Action mailed January 29, 2007, page 7.
[14] Office Action mailed January 29, 2007, page 7.

The basis for the rejection is respectfully traversed. Applicant first discusses the disclosures of the cited references separately for convenience's sake, and then addresses the combined disclosures in rebuttal of the §103(a) rejection.

Pratt

Pratt discloses the results of experiments using: 1) freeze-dried arteries from a donor rabbit in microarterial graft in a recipient rabbit (Pratt 1987) or 2) freeze-dried arteries from donor rats in microarterial graft in a recipient rat (Pratt 1986).

Neither Pratt reference discloses or suggests isolated, preserved human umbilical vessels that are directly lyophilized without chemical denaturing as required by the present claims. As to isolated, preserved human placental vessels, Pratt only make wishful statements. Specifically, Pratt 1986 states at page 628, col. 1:

> A good topic for further investigation would be the study of freeze-dried human placental vessels used as microarterial allografts. Success with such an investigation would provide a readily available source of vascular grafts without the inconvenience and additional morbidity associated with harvesting autogenous veins.

Pratt 1987 states at page 11, last paragraph:

> With the limitations of the present study notwithstanding, this new microvascular technique shows promise. Eventually, it is anticipated that freeze-dried placental or donor vessels could be used in clinical trials if future preliminary laboratory studies in rabbits and larger animals are successful.

Thus in each instance, the Pratt references, at best, make a wishful statement. Evidence of this assertion is supported by the Declaration of James R. Schneider, M.D. Under 37 C.F.R. §1.132 (the "Schneider Declaration"), Dr. Schneider, who is a co-author of each of the Pratt references, discusses the Pratt references in this Declaration at paragraphs 20-26.

Dardik.

As discussed above, Dardik fails to disclose:

- *isolating* a vessel from human umbilical cord, and
- preserving that *isolated vessel by direct lyophilization without chemical denaturing.*

Instead, Dardik, at best, discloses preserving *the entire umbilical cord* – and fails to provide any direction to preserve even the entire umbilical cord by lyophilization without chemical denaturation. Dardik also fails to disclose isolated, preserved human placental vessels.

Furthermore, as discussed in the Schneider Declaration at paragraphs 17-19, Dardik states at col.3, lines 10-22:

> **A segment of approximately 3 centimeters in length was resected from the abdominal aorta and an end-to-end anastomosis was performed between host aorta and donor umbilical vein, first using continuous 6-0 prolene suture which is a nylon monofilament suture. The distal anastomosis was then performed following flushing of the aorta to rid it of any clot material and debris. Following completion of anastomosis the distal and then the proximal clamps were removed. It was noted that there was no bleeding between the interstices of the sutures, which is unusual, and is felt to be due to the strength and self-sealing gelatinous qualities of the cord structure.**

This passage in Dardik does not instruct one to isolate the vessel from the stored umbilical cord, but rather instructs one to use a vein that is still in the umbilical cord segment. Dardik does not instruct or suggest isolating an umbilical cord vessel and preserving it separately from the umbilical cord.

The passage in Dardik above indicates that the "gelatinous qualities of the cord structure" not only provide advantages in the use of the umbilical cord vessel as a graft, but was cited as a reason for the success of the umbilical cord segment graft. As stated in the Schneider Declaration at paragraph 19, this would instruct one *not* to isolate vessels separate from the umbilical cord and preserve the isolated vessel, as such a method would not take advantage of the "strength and self-sealing gelatinous qualities of the cord structure" of Dardik's umbilical cord segment graft.

Dardik, thus, points *away* from the preserved, isolated vessel of the present claims, which preserved, isolated vessel is produced from a vessel isolated from a human umbilical cord, wherein the isolated vessel is directly lyophilized without chemical denaturing.

McDonald

McDonald only discloses a system for deploying a stent *in situ*, e.g., as reinforcement of vessel present in a patient. The only disclosure of a removable stent is in the context of a catheter for intraluminal deployment of the stent (see, e.g., For example, McDonald at col. 3, lines 51-56; col. 5, lines 25-37; col. 6, lines 38-65). In fact, McDonald discusses ways to ensure that the stent remains in place when the catheter used to delivery the stent intraluminally is withdrawn, e.g., through use of various anchors. (see, e.g., McDonald at col. 20, lines 12-33).

The combined disclosures of Dardik, Pratt, and McDonald

Upon combination of the references, the following deficiencies are noted:

- the combined references fail to teach or suggest *isolated,* preserved human umbilical cord vessels
- the combined references, at best, provide a wishful suggestion regarding freeze-dried human placental vessels; and
- the combined references fail to disclose a removable stent, or a removable stent in an isolated, preserved vessel as required by the present claims.

In fact, when the Pratt reference is read as a whole, it actually *discourages* use of freeze-dried veins as grafts. At page 628, Pratt 1986 compares the results of a prior study (Pratt et al. 1985 Microsurgery 6:211-218; "Pratt 1985") using freeze-dried veins from donor rats in allografts in recipient rats. Pratt 1986 states at page 628, col. 2:

> ing-
> %. The freeze-dried arteries were much easier to implant due to the natural rigidity in the walls, which helped to keep the lumens open during anastomosis. The walls of the freeze-dried veins readily collapsed, making anastomosis technically difficult and time consuming. There were no aneurysmal dilatations found with freeze-dried arteries as was previously reported with freeze-dried veins. All of these observations suggest that the freeze-dried microarterial allograft may be more clinically applicable than the freeze-dried microvenous allograft.

As Dr. Schneider discusses in his declaration at paragraphs 25-26, this statement in Pratt 1986 makes it apparent that results differed significantly between use of freeze-dried rat veins and use of freeze-dried rat arteries. Given that success in using freeze-direct adult rat arteries did not necessarily predict success with freeze-dried adult rat vein, one would not expect that success with freeze-dried adult rat arteries would predict success with either freeze-dried human placental vessels or with freeze-dried human umbilical cord vessels.

Moreover, due to the significant structural differences between human umbilical vessels and human adult vessels, as well as the structural differences between placental vessels and human adult vessels, as well as the susceptibility of isolated human umbilical vessels to injury, due to lack of the protection afforded by the umbilical cord sheath and Wharton's jelly, one in the field of vascular surgery would not look to umbilical cord vessels as a source for making a preserved, isolated vessel prepared by directly lyophilizing the isolated vessel (without chemical denaturing) to produce a vessel that, following rehydration, would be suitable for implantation in an adult human. This statement is supported by evidence in the form of Dr. Schneider's Declaration. See paragraphs 6-16.

In view of the above, withdrawal of this rejection is respectfully requested.

Claims 53 – Dardik and McDonald

Claim 53 is rejected under 35 U.S.C. §103(a) as being unpatentable over Dardik as applied to claim 52 above and further in view of McDonald et al. as applied to claim 27.

The disclosures of Dardik and McDonald are believed to be adequately addressed above, as are the deficiencies in an obviousness rejection based upon these combined disclosures. For sake of brevity, these arguments are not reiterated here, but are indeed applicable to claims 53 with the same effect as to the claims rejected above. It is again noted that McDonald fails to disclose a stent that is removable from a vessel. Instead, McDonald actually instructs anchoring the stent inside the vessel, as discussed above.

Withdrawal of this rejection is respectfully requested.

Claims 35-37 and 45-47 – Dardik, McDonald, Lau et al, and Chin

Claims 35-37, 45-47 are rejected under 35 U.S.C. §103(a) as being unpatentable over Pratt, Dardik et al. and McDonald et al. as applied to claims 27 and 38 respectively, and further in view of Lau et al. and Chin.

The disclosures of Dardik and McDonald are addressed above, as are the deficiencies in an obviousness rejection based upon these combined disclosures. For sake of brevity, these arguments are

not reiterated here, but are applicable to claims 35-37 and 45-47 with the same effect as to the claims rejected above. Lau et al. and Chin, which are cited for disclosure of materials and structures of stents, respectively, do not cure the deficiencies of the combined disclosures.

Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number SNDR-001CIP(SP).

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 29, 2007

By: _____
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Enclosure: Declaration of James R. Schneider, M.D. Under 37 C.F.R. §1.132 (with Exhibit)

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